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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/670,490	09/25/2003	Eytan R. Barnea	120785.0310	8761

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Pepper Hamilton LLP
Firm 21269
500 Grant Street
One Mellon Center, 50th Floor
Pittsburgh, PA 15219

EXAMINER	
CANELLA, KAREN A	
ART UNIT	**PAPER NUMBER**
1643	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/670,490	BARNEA ET AL.	
	Examiner	Art Unit	
	Karen A. Canella	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) 9-22 and 25-30 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) 9-22, and 25-30 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on May 30, 2007 has been entered.

Claims 9, 15 and 25 have been amended. Claims 26-30 have been added. Claims 9-22, and 25-30 are pending and under consideration.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 25-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 25-27 recite "having a sequence consisting essentially of" SEQ ID NO:1-12. the term "having" is construed as comprising. Thus, the metes and bounds of the claims are unclear because of the recitation of "having" before the phrase "consisting essentially of" which is midway between "consisting of" and comprising. Amendment of the instant claims to delete "having sequence" would overcome this rejection.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9-21 and 25-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the

relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 9-21 are method claims reliant n a genus of peptides "having" a sequence of SEQ ID NO:1-12 or "having" a sequence consisting essentially of SEQ ID NO:1-12. Claims 25 is drawn to a composition comprising a peptide "having a sequence consisting essentially of" SEQ ID NO:1-12. Claims 26-27 are drawn to method claims reliant a genus of peptides "having a sequence consisting essentially of" SEQ ID NO:1-12. Claims 28 and 29 are drawn to peptides and compositions comprising at least one peptide having a sequence selected from SEQ ID NO:1-12. When given the broadest reasonable interpretation "having a sequence consisting essentially of" SEQ ID NO:1-12 includes peptides minimally comprising the 7-mers of SEQ ID NO:1-12. It is noted that claims 9-21, 26-29 require that the peptide exhibits an antiproliferative activity. However, it is well known in the art that antiproliferative activity can be induced by a variety of different mechanisms which providing a negative stimulatory signal to a cell (Brohult et al (WO98/52550, page 2, lines 3-22). The specification fails to describe a mechanisms by which the disclosed peptides consisting of SEQ ID NO:1-12 induce anti-proliferative activity which would relate the structure of a peptide comprising SEQ ID NO:1-12 with the mode of antiproliferative activity induced by peptides consisting of SEQ ID NO:1-12. Thus the disclosure of 12 7-mer peptides fails to adequately describe a genus of proteins minimally comprising said peptides and exhibiting "antiproliferative activity" because said genus tolerates members which act by a mechanisms completely different than the mechanisms exerted by the peptides of SEQ ID NO:1-12. One of skill in the art would reasonable conclude that applicant was not in possession of the claimed methods or products beyond those limited to peptides consisting essentially of SEQ ID NO:1-12.

Claims 9-22, and 25-30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention..

(A) As drawn to peptides having no antiproliferative activity

The instant specification states that the mixture of peptides corresponding to SEQ ID NO:1-12 possessed no inhibitory activity against MCF-7 cells, but that SEQ ID NO:2, 3and 8 possessed significant inhibitory activity, and explains that the remainder of the peptides are able to compete with the active peptides for receptor sites on MCF-7, but do not possess inhibitory activity (page 26, line 22 to page 27, line 13). The specification further teaches that out of the peptides A-M, that A, F and K exhibited significant antiproliferative activity but that "other peptides were less activity or showed no activity" (page 27, lines 6-8). Thus the specification admits that some of the peptides A-M, outside of the peptides of A, F and K, exhibit no antiproliferative activity. Applicant argues that the antiproliferative activity is demonstrated in Figure 9. This is not persuasive. Figure 9 indicates that B and C have nearly the same proliferative activity as the negative control. There is no indication of the statistical significance for the relative numbers for proliferation between the negative control and the B plus C peptides. In light of the specification admitting that some of the peptides show no antiproliferative activity, and the lack of teachings regarding the statistical similarity or difference between the antiproliferative activity of peptides B combined with C relative to the negative control, it would be reasonable to conclude that peptides B and C have no antiproliferative activity. One of skill in the art would be subject to undue experimentation in order to carry out the method of claim 9-21, 26 and 27, or use the products of claims 28 and 29 with peptides other than SEQ ID NO:2, 3 or 8. One of skill in the art would also be subject to undue experimentation in order to use the peptides corresponding to the peptides of B and C which would include peptides of SEQ ID NO:1, 4-7 and/or 9-12 because said peptides would not be expected to have anti-proliferative activity. Further, with regard to the product claims 22, 25 and 30 it is noted that the specification fails to provide an alternative use for a peptide which is not an antiproliferative peptide, and therefore one of skill in the art would be subject to undue experimentation is order to use all the peptides claimed beyond those of SEQ ID NO:2, 3 and 8.

(B) As drawn to the administration of the peptides to a non-experimental subject

Further, the specification teaches that the antiproliferative ability of the low molecular weight peptides was quantitated in an MCF7 assay. This fails to provide a nexus with a method of treatment of a subject having cancer or a viral infection. The art recognizes that many compounds can show favorable activity in vitro but fail to show favorable activity in a clinical

treatment. Mohanlal (WO0240717) teaches that an important reason for the high failure rate in clinical trials is the poor predictive value of currently used screening technologies for biological validation, pharmacological testing, and screening for success or failure of chemical entities and biologicals in clinical trials involving human subjects, which include screening based on in vitro assays, which inadequately represent the clinical disease phenotype of the patients in which the tested chemical entities or biologicals are intended to be used in the future. Mohanlal teaches that success of chemical entities or biologicals in cell screens does not necessarily translate into clinical success in patients because the majority of chemical entities or biologicals, while successful in said cell screens fail in clinical trials, particularly in late phase II and phase III trials for pharmacodynamic reasons (lack of efficacy and/or an unacceptable adverse event profile); and pharmacokinetic reasons.

The art teaches general problems with the administration of peptide and protein drugs, namely short half-life in vivo, necessitating multiple administrations (Johnson and Tracey, 'Peptide and Protein Drug Delivery', In: Encyclopedia of Controlled Drug Delivery, Vol. 2, 1999, pages 816-833). The art teaches that major stability, release and manufacturing challenges" (page 816, second column, lines 1-5) must be met in order to overcome the technical difficulties associated with the delivery of peptides in vivo, because of the necessity of supplying repeated or sustained dosages over time necessary to overcome the short half-life in vivo. The art teaches that considerations in formulating the delivery of repeated or sustained dosages of peptides are stabilization of the peptides from degradation in vivo, and stabilization of peptides during the manufacturing process, and the subsequent controlled release of said stabilized peptides in vivo in the appropriate quantities. The specification does not teach a means for the delivery of these small peptides to the all the disease sites encompassed by all the tumor types and viral infections claimed, such that the level of peptide is maintained for the time required to produce an anti-proliferative effect in a patient. Therefore it would be undue experimentation in order for one of skill in the art to determine a means for the delivery of the peptides to the tumor in a patient in such quantities which would be efficacious to said patient, wherein said delivery means would include how to stabilize the peptides from degradation in vivo, or during the manufacturing process, and how to release the stabilized peptides in vivo in

the appropriate quantities, in addition to how to target the peptides to the appropriate disease sites.

Given the lack of teachings on all of the above, one of skill in the art would be subject to undue experimentation in order to use the claimed peptides and composition and carry out the instant methods by administering the claimed peptides to a subject having cancer or a viral infection.

The rejection of claims 9-11, 14, 22 and 25 under 35 U.S.C. 102(e) as being anticipated by Barnea (U.S. 5,648,340) is withdrawn in light of applicants arguments regarding the original of the embryonic tissue used in Barnea '340 versus the instant invention.

All claims are rejected.

All other rejections and objections as set forth or maintained in the previous Office action are withdrawn.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10-6:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571)272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Karen A. Canella/
Ph.D., Primary Examiner
Art Unit 1643